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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,245	07/25/2003	James A. Thomson	960296.99179	4191
7590		07/11/2007		
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			EXAMINER	
			SULLIVAN, DANIEL M	
			ART UNIT	PAPER NUMBER
			1636	
			MAIL DATE	DELIVERY MODE
			07/11/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/627,245

Applicant(s)

THOMSON ET AL.

Examiner

Daniel M. Sullivan

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 13 April 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1, 3, 7, 9, 10, 12, 13, 15 and 16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 3, 7, 9, 10, 12, 13, 15 and 16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

This Office Action is a reply to the Paper filed 13 April 2007 in response to the Non-Final Office Action mailed 12 December 2006. Claims 1, 3, 7, 9, 10, 12, 13, 15 and 16 were considered in the 12 December Office Action. Claims 1, 7, 10, 13 and 16 were amended 13 April Paper. Claims 1, 3, 7, 9, 10, 12, 13, 15 and 16 are pending and under consideration.

#### *Response to Amendment and Arguments*

##### Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Rejection of claims 1, 3, 7, 9, 10, 12, 13, 15 and 16 under 35 U.S.C. 112, second paragraph, as being indefinite is **withdrawn** in view of the claim amendments.

##### Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

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the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, 7, 9, 10, 12, 13, 15 and 16 **stand rejected** under 35 U.S.C. 103(a) as being unpatentable over Priori et al. (1996) *Circ. Res.* 78:1009-1015 (the discussion herein below references the online publication, which is mailed herewith) in view of Gepstein *et al.* (*supra*; as evidenced by US provisional application 60/306,462). This rejection is maintained for the reasons set forth in the 12 December Office Action (pages 4-9) and herein below in the response to Applicant's arguments.

#### *Response to Amendment and Arguments*

In response to the *prima facie* rejection of record, Applicant has amended the independent claims such that the methods require "deriving a plurality of cardiomyocyte types by *in vitro* culture from human embryonic stem cells". Applicant contends, "[N]othing in Gepstein teaches the skilled person that a culture of differentiated hES cells would include all cardiomyocyte types." (13 April Paper, page 7.) While acknowledging that other work identified multiple cardiomyocyte types in cultures of differentiated mouse embryonic stem cells applicant contends that nothing in the cited art establishes whether cultures of differentiated hES cells would or would not likewise contain multiple types. Applicant contends that at least two factors raise significant uncertainty that multiple types would emerge in hES-derived cultures: the first, being the developmental differences between mice and humans; and the second being species-specific components support mouse and hES cells in culture and direct differentiation of those

cells. Applicant contends that cited art does not consider whether the species-specific factor profiles are available, and if so, whether they contribute, positively or negatively, to differentiation in culture of these distinct cells and further contends that species-specific differences in gestational term between mouse and human raise doubts as to whether the differentiated cells can develop further in culture to include atrial and ventricular cardiomyocyte types.

These arguments have been fully considered but are not deemed persuasive. In sum, Applicant's argument appears to be that one of skill in the art would not have a reasonable expectation of success in "deriving a plurality of cardiomyocyte types by *in vitro* culture from human embryonic stem cells" by the method of Gepstein et al.

It is first noted, that the claims do not require that all cardiomyocyte types be present in the culture, as implied in Applicant's remarks. The claims merely require that a plurality, i.e., two or more, cardiomyocyte types be derived. Furthermore, the claims do not require that the individual cardiomyocyte types be present in a defined minimum ratio. Therefore, e.g., derivation of a single nodal type cardiomyocyte per million ventricular type cardiomyocytes meets the limitations of the claims. Still further, the claims do not define the properties of that distinguish the individual cardiomyocyte types. Consequently, any difference in cardiomyocyte type, e.g., more differentiated type cardiomyocyte versus less differentiated type cardiomyocyte.

On page 8 of the 60/306,462 application, Gepstein et al. teaches that the cultures described therein contained cells that stained positive for cardiac-specific proteins which exhibited varying degrees of myofibrillar organization and sarcomeric organization evidencing distinct stages of cardiomyocyte differentiation. Therefore, Gepstein et al. does teach deriving a

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plurality of cardiomyocyte types according to the broadest reasonable interpretation of the claim limitation.

Furthermore, even if the claim were construed as requiring that the derived cardiomyocyte types be atrial, ventricular or nodal, Applicant is reminded that obviousness requires only a reasonable expectation of success; obviousness does not require absolute predictability. (MPEP 2143.02.) As discussed above, the claims do not require that the individual cardiomyocyte types be present in a defined minimum ratio and, as Applicant acknowledges, it was known in the art that multiple cardiomyocyte types are derived in cultures of differentiated mouse embryonic stem cells. Although Gepstein et al. acknowledges differences in mouse and human ES cells, Gepstein et al. further teaches, “in vitro differentiation of human and mouse ES cells appears to follow parallel pathways” (Page 14, lines 3-4 of the 60/306,462 application.) Given the art considered as a whole, one would clearly have a reasonable expectation of success in deriving a plurality of cardiomyocyte types, according to the broad constraints of the claim limitation, by the method of Gepstein et al.

Applicant’s arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand properly rejected under 35 USC § 103(a) as obvious over the art.

### ***New Grounds for Objection***

#### **Claim Objections**

Claims 7, 10 and 13 are objected to because of the following informalities: Line one of the claims has been amended to change the plural “agents” to the singular “agent”. In view of

this, the use of the plural pronoun “their” in referring to the agent is grammatically incorrect. Appropriate correction is required.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M. Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel M Sullivan/  
Primary Examiner  
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